REMARKS/ARGUMENTS

Claims 1, 3-5, 9-22, 25-40, and 78-80 are pending and stand substantively rejected. Claims 1, 78, 79 and 80 are presently amended. Claim 9 is presently canceled. Reconsideration of the claims is respectfully requested.

Support for the amendments to claims 1 and 78-80 can be found in the specification at, for example, page 61, line 1 to page 64, line 14. No new matter is introduced.

Applicants also submit herewith a supplemental ADS to conform the priority data set forth in the Preliminary Amendment filed March 12, 2004.

Rejection Under 35 U.S.C. §112

Claims 1, 3-5, 9-22, 25-40, and 78-80 were rejected under 35 U.S.C. §112, first paragraph, as allegedly lacking enablement. This rejection is traversed in part and overcome in part as follows.

The Office Action (pp. 4-6) states that the specification is enabling for one *in vitro* and two *in vivo* treatment protocols. Applicants address each of these protocols in turn.

1. *In vitro* treatment

According to the Office Action, the specification is enabling for *in vitro* methods for reducing the size of a tumor comprising mammalian cells. Applicants note that the efficacy of *in vitro* methods can be described in terms of inhibiting cell proliferation, as discussed in the specification at, for example, pages 61-64 and Figs. 1 and 2. Amended claim 79 is drawn to an *in vitro* method for inhibiting cell proliferation, and is therefore enabled by the specification.

2. First *in vivo* treatment

The Office Action states that the specification is enabling for *in vivo* methods for reducing the size of a tumor in a mammal by contacting the cells with an adenoviral vector comprising a nucleic acid encoding p53, and contacting the cells with a taxane, such that growth of mammalian cancer cells deficient in functional p53 is reduced and/or the cancer cells undergo apoptosis. Amended claim 1 is drawn to such as method, and is therefore enabled by the specification.

3. Second *in vivo* treatment

The Office Action states that the specification is enabling for *in vivo* methods for treating mammalian cancer cells by administering DNA vectors directly at cancer cells, such that growth of the cells is reduced or the cells undergo apoptosis. Amended claim 78 is drawn to such a method, and is therefore enabled by the specification.

Rejection Under 35 U.S.C. §102/103

Claims 1, 3, 4, 5, 9, 10, 18-22, 25, 26, 28, 31-33, 37, 38, and 78-80 were rejected under 35 U.S.C. §102(e) as allegedly anticipated by, or in the alternative, under 35 U.S.C. §103(a) as obvious, over U.S. Patent No. 5,747,469 to Roth et al. ["Roth"]. This rejection is traversed.

1. Section 102

According to MPEP 2131, to anticipate a claim, a reference must teach every element of the claim. In brief, the presently pending independent claims 1 and 78-80 are drawn to combination therapy with a p53 nucleic acid and a taxane. In contrast, Roth discusses combining p53 gene therapy with a limited range of DNA damaging agents (see e.g. col. 4, line 53 to col. 5, line 4). It has not been shown that the presently claimed taxane is the same as the DNA damaging agents described in Roth. In fact, Roth does not assert or even remotely suggest that effects caused by DNA damaging factors (e.g. cisplatin) are similarly caused by agents such as taxanes. No evidence has been presented to support a conclusion of biochemical equivalence between DNA damaging agents and taxanes. For at least these reasons, it is improper to conclude that DNA damaging agents such as cisplatin read on the presently claimed taxane elements.

Moreover, the presently pending claims are generally drawn to methods of treating human head and neck, ovarian, prostate, or mammary cancer cells, whereas Roth discusses treatment of lung cancer cells. It has not been established that lung cancer cells are the same, either expressly or inherently, as the presently claimed cells.

2. Section 103

According to MPEP 2142, to establish a *prima facie* case of obviousness, there must be some suggestion or motivation in the reference itself or in the knowledge generally available to the artisan, to modify the reference to arrive at the presently claimed invention.

Moreover, there must be a reasonable expectation of success. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must be found in the cited reference or in the knowledge generally available to the artisan, and not based on applicant's disclosure.

The Office Action alleges that even though Roth's method may not be identical to the presently claimed methods, any differences would be the result of obvious minor variations. Applicants disagree. Cancer is a complex disease, involving a myriad of biological events. Because of this, different types of cancer drugs have different mechanisms of action. Different classes of cells react differently to different types of drugs. Combination therapy for cancer treatment can be complex in nature, and not all combinations can be predicted to work equally effectively. It is not true that if two different types of agents could be used for cancer treatment, then a treatment that replaces one type of agent (e.g. DNA damaging factor) with another type of agent (e.g. taxane) is therefore obvious. Moreover, it is not true that if a particular type of agent could be used for treating one class of cancer cells (e.g. lung), then that particular type of agent could also be used to treat a different class of cancer cells (e.g. head and neck). Further, it has not been shown why the artisan would be motivated to modify Roth to replace the DNA damaging factor with a taxane.

Further, it has not been shown that that the artisan would have predicted a reasonable expectation of success for the presently claimed invention, simply based on Roth. According to the Office Action, Roth describes a combination having an effect that is better than two agents alone, albeit without synergism. According to MPEP 716.02(a), it is well established that evidence of a greater than expected result may be shown by demonstrating an effect which is greater than the sum of each of the effects taken separately (i.e., demonstrating "synergism"). Merck & Co. Inc. v. Biocraft Laboratories Inc., 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), cert. denied, 493 U.S. 975 (1989). Thus, in no way does Roth impacts the nonobviousness of a completely different method, involving different types of cells and different types of administered agents, where the different method provides a synergistic effect.

In sum, not only does Roth fail to anticipate the presently pending independent claims 1 and 78-80, Roth also fails to render these claims obvious. Claim 9 is canceled. Claims

3, 4, 5, 10, 18-22, 25, 26, 28, 31-33, 37, and 38 depend directly or indirectly from independent claim 1, and are therefore allowable as depending from an allowable base claim, as well as for the novel and nonobvious combination of elements they recite. Withdrawal of this rejection is respectfully requested.

First Rejection Under 35 U.S.C. §103

Claims 1, 4, and 5 were rejected under 35 U.S.C. §103(a) as obvious over Roth. This rejection is traversed.

It appears that the substance of this rejection is directed toward pending claim 4, which includes treatment with a chemotherapeutic agent, and pending claim 5, wherein the chemotherapeutic agent includes cisplatin, carboplatin, or navelbine.

Applicants reiterate that amended claim 1 is nonobvious in view of Roth, for at least the reasons discussed above in the §102/103 rejection (e.g. equivalence between cisplatin and taxane has not been established). Thus, dependent claims 4 and 5 are also nonobvious as depending from a nonobvious base claim, as well as for the nonobvious combination of elements they recite. Withdrawal of this rejection is respectfully requested.

Second Rejection Under 35 U.S.C. §103

Claims 1 and 9 were rejected under 35 U.S.C. §103(a) as obvious over Roth in view of Verma et al., Nature 389:239-242 (1997). This rejection is traversed.

Claim 9 is canceled, and amended claim 1 is drawn to a treatment method with an adenoviral vector. Applicants reiterate that amended claim 1 is nonobvious in view of Roth, for at least the reasons discussed above in the §102/103 rejection (e.g. equivalence between cisplatin and taxane has not been established). Verma does not remedy this deficiency. Withdrawal of this rejection is respectfully traversed.

Third Rejection Under 35 U.S.C. §103

Claims 1, 3, 4, 5, 9-12, 15-22, 25, 26, 28, 31-33, 37, 38, and 78-80 were rejected under 35 U.S.C. §103(a) as obvious over Roth in view of Moojoo et al., Oncogene 12:1617-1623 (1996) as evidenced by Wills et al., Human Gene Therapy 5:1079-1088 (1994). This rejection is traversed.

Applicants reiterate that amended claims 1 and 78-80 are nonobvious in view of Roth, for at least the reasons discussed above in the §102/103 rejection (e.g. equivalence between cisplatin and taxane has not been established). Moojoo and Wills fail to remedy this deficiency.

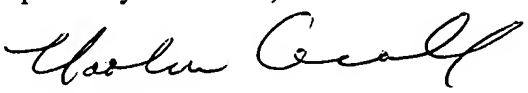
Claim 9 is canceled. Claims 3, 4, 5, 11, 12, 15-22, 25, 26, 28, 31-33, 37, and 38 depend directly or indirectly from independent claim 1, and are therefore allowable as depending from an allowable base claim, as well as for the nonobvious combination of elements they recite. Withdrawal of this rejection is respectfully requested.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 303-571-4000.

Respectfully submitted,



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